Amendments to the Claims

The listing of claims will replace all prior versions, and listings of claims in the application.

1. (Cancelled)

2. (currently amended) The method of claim [[1]] 40, wherein the lysate contains the biomolecule of interest.

3. (currently amended) The method of claim [[1]] 40, wherein the retention layer is composed of a particulate material.

4. (original) The method of claim 3, wherein the retention layer consists of glass beads.

5. (currently amended) The method of claim [[1]] 40, wherein the retention layer is composed of rigid retention material.

6. (original) The method of claim 5, wherein the retention material comprises sinter plates.

7. (currently amended) The method of claim [[1]] 40, wherein in step d), increasing pressure is applied to the mixture from the top of the clarification reactor, thereby ensuring a constant outflow of the lysate.

8. (previously presented) The method of claim 7, wherein pressure is increased by applying pressurized air.

9. (original) The method of claim [[1]] 40, wherein one or more wash steps are inserted between steps d) and e).

10. (canceled)

11. (currently amended) The method of claim [[1]] 40, wherein the flow of the cell suspension and the flow of the alkaline lysis solution are combined, without further mixing, before entering the lysis reactor, thus forming a single flow that is thoroughly mixed when flowing through the particulate material in the lysis reactor.

12. (currently amended) The method of claim [[1]] 40, wherein the cell suspension and the lysis solution are introduced into the lysis reactor in the form of two independent flows.

13. (currently amended) The method of claim 12, wherein said two flows are introduced ~~through inlets that are situated close to each other~~ from independent sources through T-type or Y-type connectors, thus forming a single flow.

14. (previously presented) The method of claim 12 or 13, wherein said two flows are transported at a defined ratio of flow rates, thereby ensuring a constant ratio of cell suspension and lysis solution volumes.

15. (currently amended) The method of claim [[1]] 40, wherein in step c), the lysed cell solution obtained in step b) is mixed with a neutralizing solution in a continuous mode.

16. (previously presented) The method of claim 15, wherein the lysed cell solution and the neutralizing solution are combined at a constant ratio of flow rates.

17. (currently amended) The method of claim [[1]] 40, wherein a concentration and/or a conditioning step is inserted between step d) and step e).

18. (previously presented) The method of claim 17, wherein a concentration step and a condition step are inserted, and wherein said concentration step takes place before said conditioning step.

19. (currently amended) The method of claim [[1]] 40, wherein said biomolecule of interest is a polynucleotide.

20. (currently amended) The method of claim 19, wherein the polynucleotide is plasmid DNA.

21. (canceled)

22. (canceled)

23. (currently amended) The method of claim [[1]] 40 wherein, in addition, step a) is operated in a continuous mode.

24. (currently amended) The method of claim [[1]] 40, wherein the host cells obtained in step a) are cryo-pelleted.

25. – 39. (canceled)

40. (new) A method of producing a biomolecule of interest using an automated or semi-automated device comprising:

a) cultivating host cells to produce the biomolecule of interest and optionally harvesting and re-suspending the cultivated host cells;

b) introducing the cell suspension and the lysis solution into a lysis reactor at a defined ratio of flow rates and disintegrating the host cells by alkaline lysis in an alkaline lysis reactor containing a particulate material;

c) neutralizing, in a neutralization reactor, the alkaline lysate and precipitating cellular debris and impurities, wherein the neutralization reactor is fluidly connected to the akaline lysis reactor and the lysis solution is mixed with the neutralization solution in a neutralization reactor;

d) separating, in a clarification reactor, neutralized lysate containing the biomolecule of interest from the precipitated cellular debris and impurities, wherein the neutralization reactor is fluidly connected to the clarification reactor and allows the lysate to flow through the clarification reactor containing a retention material, and said retention material functions to retain the precipitate on top and within the retention material while allowing the purified lysate to flow from the clarification reactor; and

e) purifying the biomolecule of interest,

wherein said method is operated on a manufacturing scale.

41. (new) The method of Claim 40, wherein one or more distribution means are employed to reach the surface of the retention layer and evenly distribute a mixture of precipitate and lysate as obtained in step c) into the clarification reactor of step d).